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Introduction. Chronic peptic ulcer of the duodenum is a common disease. It causes the loss of over two million working days per annum in the UK. In Scotland, its sufferers occupy over one hundred thousand bed days, and, along with benign gastric ulcer it kills almost four hundred Scots per year.[1,2] By the age of fifty about ten per cent of the male Scottish population will have been affected by it.

If it is not rare, neither is it new. The term peptic ulcer was first used in 1882 by Quincke, believing that pepsin was the prime culprit. Bilroth first performed his operation in 1881, so we have nearly a century of operative experience to draw from.

Yet, despite this, there is still controversy over how this condition should be managed. Until recently our drug therapy was ineffective in altering the natural history of the disease, and even now has little place in recurrent ulceration. And trying to untangle the mass of surgical literature with many surgeons each promoting the virtues of one of the various manoeuvres, with at least nine major and a multitude of minor variants on offer, is not easy.

And why should this be? Largely because we still do not fully understand its multi-factorial aetiology, when applied to the individual. Many factors have been implicated, most now well founded, but some still a little dubiously, but we are still not in a position to relate these to each patient, and treat his disease specifically, even if we had the means. And on the surgical side the differing emphasis placed on the balance between effectiveness and sequelae, both morbid and mortal, compounded by the natural variations between surgeons' tachniques and abilities, as well as patient variables have served to muddy the waters for those seeking clear cut answers.

However, in the last few years new developments have arisen, both in the medical and surgical managements which promise to radically improve the outlook for our patients. The advent of Histamine H_2 receptor antagonists has given us a potent and specific means of reducing acid secretion, and the development of Highly Selective Vagotomy offers a less ablative approach with a marked reduction in the side effects so long associated with gastric surgery, and it is on these that I shall concentrate in this essay.

Uncomplicated Chronic Duodenal Ulcer

Conventional wisdom has it that the initial management of duodenal ulcer, in the absence of life threatening complications, should be conservative in all cases, and nothing has appeared in recent years to change this.

Admission to hospital is preferable, as bed rest still remains a corner stone of therapy and the release from domestic tensions and pressures may aid this. This alone is enough to bring relief of symptoms within a few days to many patients, a fact which must be borne in mind when assessing the efficiency of drugs. Eighty per cent of patients will remit symptomatically for a greater or lesser period without specific treatment.

Stopping smoking has been proven to speed healing of gastric ulcers, but the evidence in duodenal ulcer is less conclusive. Empirically, however it seems sensible and is

retained by most clinicians.

As for diets, the milk-fish diet of the past has been discredited, with hourly milk feeding having shown to increase acid secretion, and no evidence of increased healing being found. Dietary advice should now be limited to avoiding those foods and alcohol which aggravate symptoms and to take regular smallish meals.[3]

Drug treatment has evolved considerably in recent years, and there is now much evidence that healing can be accelerated as well as symptoms alleviated. The drugs available fall into five categories according to site of action.

1) Antacids. Providing purely symptomatic relief, these were the main stay of treatment until the newer drugs arrived, and remain useful adjuvant therapy for relief of symptoms, and should be allowed freely.

Total titration of gastric acidity is neither practical[4] nor neccessary. What is required is rapidity plus freedom from side effects, which is best achieved by balancing the cathartic and constipating effects of magnesium and aluminium compounds.

2) Anticholinergics. Many and various yet differing little in their effects or side-effects. They are less effective than antacids for symptoms and have no evidence for a healing action.[5] Since their role in maintenance therapy for the prevention of recurrence is also contested[5] they must be of declining usefulness in today's treatment.

3) Antipepsins. These synthetic sulphated mucopolysaccharides eg. amylopectin are claimed to interfere with auto digestion by pepsin. They are very expensive and not generally available, though they may have an effect on recurrence,[6] again disputed[7] and requiring further evaluation.

4) Mucosal Barrier Fortifying Agents. The first of the new generation compounds, this group has three contenders. Carbenoxolone,[15] a liquorice derivative, whose mode of action is not clear, but which may stimulate mucus producti on. When it first appeared it produced very poor results in duodenal ulcer (Doll,1962), though effective in gastric ulcers, but it has recently been re-examined in the belief that effective concentrations had not been realised in the duodenum previously, and now a degree of endoscopically proven healing has been shown.[5] But it has serious disadvantagesin terms of side effects producing salt and water retention and potassium loss. Conventional diuretics worsen the potassium loss and spironolactone blocks its therapeutic effect also, which must limit its use in duodenal ulcer.

Deglycyrrhinized liquorice has not been shown to speed healing, but chelated Bismuth has to a minor degree.[5]

5) Histamine H_2 Antagonists. Histamine is thought to be an intermediate messenger in the acid and pepsin secreting pathway in the gastric mucosa both for vagal and gastrin stimulated secretion. The receptor for this is pharmacologically differnt from that mediating bronchial and smooth muscle contraction and is designated H_2. The first drug to be developed was Burimamide which was shown experimentally on dogs to reduce acid secretion. It lacked potency however and could only be given parenterally, and was replaced by Metiamide which was put on trial. The largest published trial was the International Multicentre Trial[8] which followed sixty seven patients with endoscopically confirmed duodenal ulcer in a metiamide v. placebo randomised controlled trial.

Ulcer healing in six weeks was significantly increased compared to placebo (Table 1). It also produced a statistically significant reduction in antacid consumption and daytime pain, measured by a self scoring system.

This difference was greater than has been shown for the other groups of ulcer healing drugs.

	% endoscopically proven healing at six weeks	
Placebo	25	
Metiamide 1g/day	62	67
Metiamide 1.3g/day	73	

Table 1

However Metiamide had several side effects, the most serious of which was bone marrow depression which led to one death. This led to the toxic thiourea group being replaced by a cyanoguanidine group and the new drug cimetidine was released for trial.

The results published so far seem to indicate that cimetidine is both effective and free from major side effects though of course it will be some time before the latter can be stated categorically.

Pouder[9] produced complete healing in all of a series of ten patients on cimetidine 800 or 1600mg/day, for six weeks. Heggie[10] produced healing in seventeen of nineteen patients (90%), on 400mg t.d.s. Bodemar and Walan[11] showed ninety per cent healing ina series of forty-four patients, as against thirty-six per cent on placebo, on a regime of 200 or 300mg q.d. They also followed acid secretion, antacid consumption and self assessed symptoms and found a statistically significant reduction in all three. Marginally better results were found on the higher dose.

Cimetidine has undoubtably been a great breakthrough. These series showed ulcer healing and symptomatic relief in ninety per cent of patients, a far better result than has been achieved by other drugs. Antacids failed to heal ulcers faster than methyl cellulose, the control chosen for one trial.

However, one major problem still remains, namely that of recurrence, since the now standard six week cource does not alter the natural history. In the series by Heggie[10] above seven of his seventeen patients with healed ulcers had a recurrence within a month of stopping treatment. Trials of continuous cimetidine, as a prophylactic measure on a dose of 400mg/day, taken at night, are now under way, but early results indicate that this is not fully effective.[12]

Fortunately cimetidine, being as yet free from side effects, may, with long term therapy (for life?), offer an answer to recurrence for many sufferers, but evaluation of this is based on a few trials with small numbers of patints followed for relatively short periods, and an answer cannot yet be given.

Therefore, the treatment of recurrent or persistent ulceration is still surgical. The indications, which have not altered for some time, are reasonably clear. They are:

a) intractable pain, or recurrence of pain with frequent loss of work
b) complications - pyloric stenosis, perforation or bleeding
c) presence for five years or more.

The last is a little more controversial but it has been stated that an ulcer present for five years is unlikely to heal and that the risk from complications of having an ulcer for five years is similar to that of an operation.

The present authors of "Bailey and Love" suggest that patients should "earn" their operation, since unless they have suffered from some pain or a complication they may be ungrateful if significant symptoms arise from surgery. But this may change at least in degree in future years if recent developments hold good.

Having decided on surgery, the choice is wide and a short survey of the alternatives may be useful. The aim of operation is to reduce the amount of acid bathing the duodenum which can be achieved by bypassing it, removing a part of the secretory apparatus or by removing the stimulus to secretion both neural and endocrine.

The earliest operations were gastrectomies with duodenal or jejunal anastomosis. This was fairly effective but had numerous side effects and a high mortality. Sectioning of the vagi at the oesophageal hiatus was introduced, thus removing both direct and gastrin mediated secretion. However the vagi control gastric emptying and gastric stasis was produced neccessitating a drainage procedure either by pyloroplasty (at least four methods), gastrojejunostomy or antrectomy which also has the virtue of removing the gastrin mediated stimulus to secretion.

By the mid sixties many surgeons had become dissatisfied with the unsatisfactory results. Many variants had been tried but despite long experience few good results were obtained and new ways to deal with the problem were sou ght.

With titles like 'The Surgeon's Dilema' [1] the papers of the period set out the problem. Partial gastrectomy had the lowest recurrence rate but serious side effects and a significant mortality. Vagotomy and drainage was safer but had a higher recurrence rate and a different though no less debilitating set of side effects.

This led to the development of a selective vagotomy to overcome some of the post vagotomy symptoms by leaving intact the hepatic and coeliac branhes, and most recently a highly selective vagotomy which leaves the antrum innervated as well, allowing normal gastric emptying so that no drainage procedure is neccessary.

The reasons for dissatisfaction were not hard to see. Table 2 lists the incidence of side effects and recurrence found in four of the more popular procedures. Five hundred and eight patients were followed for five to eight years in the Leeds York trials.[13,14] Uncharacteristically this series produced only one operative death (in the truncal vagotomy and pyloroplasty group) partly due to selecting out of high risk patients and partly due to the great experience of all the participants.

Similar results were obtained in Glasgow[15] and in America by the Veterans' administration who followed 1357 patients.[16] These results showed that only major gastric resection carried a higher mortality- nearly 2% as against 0.6 - 0.9% for other operations. With their low mortality they pointed towards truncal vagotomy

Symptom	Vagotomy and gastro-enterostomy n=119	Vagotomy and antrectomy n=116	Subtotal gastrectomy n=107	Vagotomy and pyloroplasty n=164
Epigastric fulness	40.2	36.3	36.5	37.1
Early dumping	17.9	8.6	21.5	11.9
Late dumping	6.0	4.3	0.9	1.9
Nausea	12.8	17.2	23.4	17.6
Food vomiting	4.3	9.6	5.6	4.4
Bile vomiting	14.5	13.8	13.1	10.1
Heartburn	19.8	15.7	8.4	12.6
Flatulence	17.9	22.8	19.8	20.1
Dysphagia	1.1	0.0	0.0	0.6
Reflux	4.0	7.0	4.3	-
Diarrhoea	26.3	23.2	6.5	21.7
Degre e of certainty of recurrence				
Proven	3	0	1	11
Suspected	4	2	1	7
Very dubious	3	4	3	5
Total	3-10	0-6	1-5	11-23

Table 2

and gastro-jejunostomy or antrectomy as the best operations in experienced hands and called for a halt in the drift towards vagotomy and pyloroplasty which was steadily growing in popularity due in part to its more physiological approach.

Nevertheless this still produces a considerable and unacceptable burden of sequelae, even in the best hands.

The first major trial of selective vagotomy was by Kennedy in Belfast who followed one hundred patients with truncal vagotomy and drainage or selective vagotomy and drainage and produced a reduction in post operative diarrhoea from 30% to 8% a statistically significant result (a rare event in most of the surgical papers on duodenal ulcer), with similar results for recurrence and other symptoms.

Most attention soon turned however to highly selective vagotomy which on a theoretical basis offered much by not interfering with gastric emptying and by not requiring the alimentary tract to be opened. It was first performed as early as 1957 by Griffith and Harkins on an experimental basis but they included a drainage procedure. Andrup in Copenhagen and Johnston in Leeds were the first to perform it without drainage. Soon many people were trying it and reporting their results which, often, were very poor for a number of reasons. But many of these bad early results pointed to errors of technique and procedure and are worth looking at.

One major early fault in technique was an incomplete oesophageal clearance and this was illustrated by poor results in a number of studies. Kronberg in Copenhagen[18] produced excellent results for dumping, diarrhoea and epigastric fulness but a recurrence rate of 22%, after one year. Hellenbeck[19] in America managed to reduce their incidence of recurrence from 15.4 to 6% (one from seventeen) by increasing their oesophageal skeletonisation from two to seven and a half centimetres above the cardia. Similarly, another study by Kronberg[20] compared four techniques for the operation with lower recurrence when the oesophagus was adequately cleared, finally

adopting the technique of Goligher which was superior for both recurrence and symptoms.[21] Another problem, shown by Sohlaurg in Bergen passes a comment which is pertinent to most of what has been discussed so far, namely that good results depend on experienced operators. The Bergen study included a large number of junior operators some of whom had only assissted at one such operation before undertaking it themselves. Though few of their results could be considered good, they steadily worsened with the increasing inexperience of the operators. It must be remembered that most of the good results both for the more established and the more recent operations have been obtained by very experienced surgeons with a special interest in, and performing large numbers of, the particular operation and so their results will be hard to repeat, though this is balanced, in part at least, by the fact that the new operation is young and should improve with age as has been the case with most procedures as further improvements in fine technique are developed.

In order to assess the place of highly selective vagotomy (HSV) in the modern management of duodenal ulcer, we must have the answers to three questions;

i) is it safe?

ii) what are its post operative consequences?

iii) is it effective?

Its safety is least in doubt. Johnston in Leeds[22] sent a questionnaire to all the surgeons he knew to be doing HSV's and received replies covering 5539 patients. This showed an overall mortality of 0.31%, compared to 0.8% in6490 cases of truncal vagotomy and drainage, and 1.6% in 1725 cases of truncal vagotomy and antrectomy from other collected series. The only specific mortality related to this operation was from upper gastric necrosis which accounted for five deaths (0.09%), and prompted Johnston to advocate the reperitonisation of the lesser curvature as well as careful preservation of vascalature not sacrificed neccessarily in the procedure.

Reports of post operative sequelae vary, but largely agree that they are significantly less than for other procedures.

Author	No. of patients	Period of follow-up (yrs.)	Incidence of - (%) Recurrence	Dumping	Diarrhoea
Grassin	787	1-6	1.1	0.4	0
Hedenstedt	465	0.5-7	1.0	2.0	0
Liarag	265	3-6	6.0	2.0	2.0
Goligher*	250	2	1.0	7.0	2.0
Holst-Christeson	160	1-4	9.0	Not severe	
Kennedy	112	mean 2.2	6.0	7.0	2.0
Lyndon*	100	5	1.0	-	-
Sayers*	84	0.5-4	1.2	1.0	1.0

Table 3 Taken from Andrup[23] except for * (24-26).

THe figures in Table three for incidences of diarrhoea and dumping compare extremely favourably with those in Table 2. The problem of poor drainage leading to epigastric fullness and gastric stasis was anticipated, but reports vary enormously. Goligher puts epigastric fullness at 29%, Sayers at 8% but Goligher claimed that all but one of his patients could eat a normal meal without discomfort. Johnston's mammoth collected series put gastric stasis, both early and late, at 1.3%, with a reoperation required to provide drainage in 0.8%. Barium and other studies have shown that in general liquids drain a little faster than usual and solids a little slower.

The series by Lyndon also showed that, although all their patients gave a negative Hollander test one week post operation, this was rapidly changed to a positive rate of 94% after three years. However, the level of peak acid output on insulin stimulation was only 10% of the pre-op level, and offered no prognostic indicator for recurrence.

The incidence of recurrence with this operation in general is still not clear. Since it probably takes two to three years for a surgeon to familuarise himself with the operation and perfect his technique before he can reasonably compare it with his performance of more established procedures, and then takes at least five to ten years of follow up before reliable rates of recurrence can be established, and since no one has this length of experience, it would be foolish to make a final judgement on figures now available. Nevertheless some inferences can be drawn.

Table 3 also shows recurrence rates for most of the large series published to date and these vary from 1 - 9%. Undoubtably these figures will rise with time as the follow up lengthens. The best result (1% at 5 years by Lyndon) compares very favourably with any other method but in general this has not been widely achieved. We can say for certain that it will not prove as effective as vagotomy and antrectomy or larger gastric resections but that it could equal results for vagotomyand gastro-jejunostomy and will probably be more effective than vagotomy and pyloroplasty. Comparisons with selective vagotomy and drainage are few, but four randomised controlled trials reported by Andrup[23] suggest near parity on recurrence but a strong advantage for the highly selective procedure as regards sequelae, though these again suffer from small numbers and a short follow up.

Thus, HSV offers an attractive proposition to those favouring minimal intervention in the first instance, being very safe and largely free from side effects, and who consider acceptable the possibility of a slightly higher incidence of recurrence perhaps neccessitating a further operation at a later date. Those who consider surety as the prime consideration must opt for one of the established procedures with vagotomy, preferably selective, plus antrectomy offering probably the best choice. If it were I on the table, I would want a surgeon of the former kind.

Summary

On confirmation of the diagnosis of duodenal ulcer medical treatment should be instituted. This will consist of bed rest, stopping smoking, a minimally altered diet and drug therapy in the form of cimetidine 1.3 g/day in divided doses with additional antacids as required. This will produce healing in about 90% of cases

within six weeks. Thereafter cimetidine 400 mg/day may be useful as prophylaxis. For persistant or recurrent ulcers (or for complications, with which I have not dealt here) surgical treatment is required. The choice of operation will continue to depend on the surgeons preference but the new operation ofHSV, if it maintains or improves its reliability as it develops, must continue to grow in popularity, offering as it does both greater safety and greatly fewer post operative symptoms.

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